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Inability to Predict Relapse in Acute Asthma

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INABILITY TO PREDICT RELAPSE IN ACUTE ASTHMA

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FISCHL and co-workers developed an index that they claimed would predict relapse in patients with asthma.[1] The index had a 95 per cent sensitivity and a 97 per cent specificity when applied to a sample of emergency room patients discharged or hospitalized within 12 hours. The authors enumerated the advantages of this index, including cost-effectiveness and a shorter period of emergency care before hospitalization. Other investigators have reported that the index is both accurate[2] and useful.[3]

Before this or any other index gains universal acceptance, we should demonstrate that the predictions are valid in a variety of settings.[4,5] This validation should be performed with different observations from those used in the model's derivation.[4,6,7] Until such validation has been achieved with a different, or test, set of data, one cannot confidently rely on the index.

Because of the potential benefit of a predictive index for relapse of asthma, we studied emergency room patients with acute asthma. We could not develop an index for predicting relapse in our patients. Moreover, we failed to confirm the predictive accuracy of the index developed by Fischl and colleagues. These findings cast doubt on the utility of the index in our emergency room and, therefore, raise questions about its use in other settings.

Methods

We collected data on 114 patients with asthma who were seen at the Medical College of Virginia emergency room. Collected data included the seven signs and symptoms that make up Fischl's index (Table 1). Senior medical residents and emergency room attendants made decisions to discharge or admit patients on the basis of a clinical evaluation. The emergency room physicians recorded demographic data (age, race, and sex), the discharge status (admitted or discharged), the time spent in the emergency room before discharge, and whether the patient was given a prescription for steroids at discharge. One of us (J.P.W.), a physician's assistant, contacted patients 7 to 10 days after discharge to determine whether there had been a relapse, as indicated by a repeat emergency visit to a physician or hospital for treatment of asthma.

Neither admission/discharge decisions nor treatment plans were governed by protocol. The emergency room physicians decided on discharge medications and follow-up arrangements. The maximum allowable duration of emergency care was 24 hours.

Predictor-index scores were calculated using Fischl's formula. Scores were tabulated for each of three groups: patients who were successfully treated, those who had a relapse, and those who were admitted. Sensitivity and specificity were calculated by standard formulas.[8] A highly sensitive index would identify with high probability the patients most likely to have a relapse or to be admitted, whereas a specific index would identify those unlikely to have relapse or to be admitted. We also plotted a receiver-operating-char-

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Table 1. Scoring System for the Predictor Index.

Factor *	Value for a Score of 0	Value for a Score of 1
Pulse	<120	≥120
Respirations	<30	≥30
Pulsus paradoxus	<18	≥18
PEFR	>120	≤120
Dyspnea	Absent or mild	Moderate or severe
Accessory muscle use	Absent or mild	Moderate or severe
Wheezing	Absent or mild	Moderate or severe

*The values for the seven factors are added to obtain the index score.[1] PEFR denotes peak expiratory flow rate.

acteristic (ROC) curve using each of the eight possible index scores as a positive test.[9] For each value of the test, the ROC curve shows the proportion of patients with true-positive tests (plotted on the ordinate) as compared with the proportion with false-positive tests (on the abscissa). If the results of a test are random, then both proportions are roughly equal for all values and the ROC curve is a straight line with a slope of one. A useful test has an ROC curve that rises rapidly and then reaches a plateau. The point of inflection represents the test score at which the ratio of true-positive to false-positive results is highest and is therefore the score most commonly used to define a positive test.

We examined the relation of the patient's initial index score to the likelihood that the patient would receive a prescription for steroids at discharge, as well as to the probabilities of admission and relapse. These relations were tested with Kendall's tau (a nonparametric correlation coefficient).[10] Finally, using logistic regression, we tried to develop a formula for the prediction of relapse in our patients.[11]

Results

We collected data during 114 patient visits. Seventy-six patients were 45 years of age or younger, and 37 were older than 45 years, which was the age limit used in the construction of the original index.[1] Twenty-eight patients were excluded from the analysis because of incomplete data collection (17 were 45 years or younger). Index scores for the three groups are shown in Table 2. The scores for patients younger than 45 years are shown in Table 3. We found no differences between the younger and older patients in terms of either index scores (chi square, 8.566 with 6 degrees of freedom; P = 0.1995) or group distribution (chi square, 0.223 with 2 degrees of freedom; P = 0.8946).

Table 2. Index Scores for 86 Patients with Asthma.

Index Score	Successfully Treated Group	Relapse Group	Admitted Group
	number of patients		
7	0	0	0
6	2	0	0
5	3	0	3
4	5	2	6
3	7	1	7
2	8	2	1
1	13	2	0
0	19	4	1
Missing data	18	3	7

Sensitivity and Specificity of the Index

With a score of 4 or higher considered a positive test, we calculated the sensitivity and specificity of the index. The sensitivity for predicting hospital admission was 50 per cent, whereas the specificity was 82.4 per cent. When the test was used for predicting relapse, the sensitivity was only 18.1 per cent, with a specificity of 82.4 per cent. The decreased sensitivity and specificity for predicting relapse were not secondary to the use of a particular score. The ROC curve in Figure 1 shows that no index scores were useful in our discharged patients.

Index Scores

Despite the low sensitivity of the index, the probability of admission did increase as the index score increased (Kendall's tau, 0.37137; P = 0.0001). However, the probability of relapse did not correlate with the initial index score (Kendall's tau, −0.0187; P = 0.8640). Both steroid prescriptions at discharge and index scores were recorded for 50 patients. Higher index scores were associated with a higher probability of discharge with a prescription for oral steroids (Kendall's tau, 0.3703; P = 0.001).

Table 3. Index Scores for Patients 45 Years of Age or Younger.

Index Score	Successfully Treated Group	Relapse Group	Admitted Group
	number of patients		
7	0	0	0
6	2	0	0
5	2	0	2
4	4	1	5
3	2	1	3
2	4	2	1
1	10	1	0
0	15	3	1
Missing data	10	5	2

Logistic Regression

We could not distinguish the relapse group from the successfully treated group by logistic regression. None of the variables noted above significantly predicted relapse in our patients.

Discussion

The ability to predict relapse accurately in patients with acute asthma might affect management decisions. Practitioners might "prophylactically" admit patients in whom relapse was expected, and investigators could test strategies for outpatient management (e.g., oral steroid therapy) to lower the relapse rate.

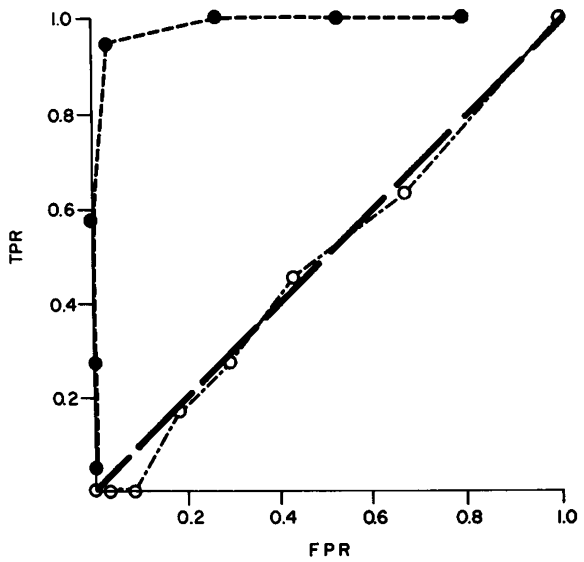

Figure 1. Receiver-Operating-Characteristic Curves for the Original Data and for Our Data.

The false-positive rate (FPR) is on the abscissa; the sensitivity, or true-positive rate (TPR), is on the ordinate. The original data (represented by solid dots) indicate a very high sensitivity and a very low false-positive rate, and therefore, a very high degree of accuracy. Our data (open circles) show that the sensitivity and false-positive rate are essentially equal, indicating a lack of discrimination. The heavy broken line indicates the equality of FPR and TPR.

Unfortunately, the present study neither confirms the accuracy of Fischl's index nor allows us to establish our own predictive index.

The emergency room physicians in our study apparently perceived patients with higher index scores as having more severe asthma attacks. Both the probability of steroid prescription and the likelihood of admission increased with higher index scores. These findings support the contention that the score on the Fischl index indicates to some degree the severity of asthma. However, in our discharged patients, it did not differentiate the relapse group from the successfully treated group. Thus, we cannot recommend the index for making discharge or admission decisions.

There may have been differences in treatment between the two studies. Whereas Fischl et al. did not comment on the outpatient use of steroids in their study group, we treated many of our patients with short-term steroids. Several authors suggest that oral steroid therapy may prevent continued bronchospasm in patients with severe acute asthma.[12-15] Liberal use of steroids may help explain the results in our patients whose initial index score was 4 or above.

We did not standardize therapy by protocol; the emergency room physicians in our study used individualized therapy. When patients were not progressing as expected, the treatment plan could be and often was changed. Clinical progress should influence management, and changes in management should alter clinical progress.[16]

At the Medical College of Virginia emergency room 24 hours is the maximum duration for emergency care. This rule permits a relatively long period of intensive therapy before the decision is made to admit or discharge a patient. Many of our patients stayed in the emergency room longer than the 12-hour maximum reported by Fischl et al., and this longer observation period may have been an important factor.

Patients with asthma have a relapse for a variety of reasons, not all of which are related to the severity of illness. Some patients return to the emergency room because of nonmedical factors, and others because of poor compliance. Other possible factors include reexposure to allergens, inability to afford expensive medication, and inadequate prescriptions at discharge. These factors may differ from city to city and may be secondary to cultural, ethnic, or regional differences. One would expect that both management after discharge from an emergency room and duration of emergency treatment are important factors in determining the relapse rate.

It seems likely that no index will be able to predict relapse accurately in patients with asthma in a variety of settings. Relapse is not a simple phenomenon with only one cause but a complex matter related to the severity of asthma, treatment, compliance, and psychosocial factors. Discriminant analysis and other classification techniques should work best when the predicted outcome can be clearly defined. Good examples of such outcomes include myocardial infarction, a positive throat culture, and gallstone composition.[17-19] To expect a reproducible prediction of such a multifactorial event as relapse may be unreasonable. It is not surprising that we could not predict relapse and successful treatment in our patients on the basis of initial findings; we doubt that anyone will be able to make a valid prediction.

Certainly, Fischl's index correlates with the severity of asthma, as reflected by the tendency for admissions to increase with higher scores. Unfortunately, however, the index does not help with decision making in the emergency room. Physicians must continue to weight many factors — not all quantifiable — in making decisions concerning admission.

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CASE RECORDS
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CASE 9-1984

PRESENTATION OF CASE

A 64-year-old man was admitted to the hospital because of hypoglycemia and a thoracic mass.

He was in excellent health until two months earlier, when he began to have morning headaches, which were relieved by eating breakfast. Eleven days before admission he went on vacation and drank several glasses of beer that evening. The next morning he could not be aroused from sleep. He was taken to a hospital, where glucose was administered by vein, and he soon became alert. A specimen of blood, drawn before the injection, showed that the glucose was 32 mg per 100 ml (1.8 mmol per liter). X-ray films of the chest (Fig. 1) showed a mass, 9 by 13 cm, in the right lower hemithorax, with a small right pleural effusion. A ^{99m}Tc sulfur colloid liver–spleen scan was negative. A computed tomographic (CT) scan of the brain, performed with the injection of contrast material, was negative. A CT scan of the thorax and abdomen (Fig. 2) disclosed a soft-tissue density in the right posterior hemithorax, which extended from the level of the tracheal carina to the diaphragm, with questionable necrotic changes; no bony erosion was observed. An ultrasound examination of the chest showed an anechoic area, believed suggestive of loculated pleural fluid. Attempts at needle biopsy of the lesion were unsuccessful. An infusion of glucose was administered during the course in the hospital, and blood glucose levels ranged from 75 to 98 mg per 100 ml (4.2 to 5.4 mmol per liter). During temporary interruption of the glucose infusion the glucose was 32 mg per 100 ml (1.8 mmol per liter), and the plasma insulin 12 μU per milliliter. He was referred to this hospital.

The patient was a retired stockbroker. He gave a 40-pack-year history of cigarette smoking and drank small amounts of alcohol. Viral hepatitis occurred 41 years before entry and again 5 years later. An x-ray film of the chest obtained seven months before admission was reported to be normal. The patient's father had carcinoma of the prostate gland. There was no history of cough, hemoptysis, fever, chills, thoracic or abdominal pain, anorexia, diabetes mellitus, use of medications, prior confusion or loss of consciousness, seizures, weight loss or gain, chronic liver disease, radiation treatment to the head or neck, or exposure to asbestos except that he served on a destroyer during World War II. There was no family history of endocrinopathy.

The temperature was 36.9°C, the pulse was 70, and the respirations were 20. The blood pressure was 170/90 mm Hg.

On examination the patient appeared thin but well; no cushingoid features were noted, and skin pigmentation was normal. No lymphadenopathy was found. The head was normal. The right thyroid lobe contained a single nodule, 1 by 2 cm, that was smooth and firm; the left lobe was questionably enlarged. Dullness and diminished breath sounds were noted over the lower half of the right hemithorax; a loud systolic bruit was heard 7 cm to the right of the spine at the level of the 10th dorsal vertebra; an area of nontender fullness was palpated over the region of the bruit. The left lung was clear, and the heart was normal. The edge of the liver descended 3 cm below the right costal margin, with a vertical span of 10 cm; no splenomegaly or mass was found. There was no peripheral edema or clubbing. Rectal and neurologic examinations were negative.

The urine was normal. The hematocrit was 50.9 per cent; the white-cell count was 9300, with 67 per cent neutrophils, 25 per cent lymphocytes, 6 per cent monocytes, 1 per cent eosinophils, and 1 per cent ba-